Master of Science Program
«Research Methodology in Biomedicine, Biostatistics and Clinical Bioinformatics»

School of Medicine
School of Health Science
University of Thessaly

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Master of Science's Thesis

«COAGULATION PROFILE AND OUTCOME OF ENDOVASCULAR REPAIR FOR RUPTURED ABDOMINAL AORTIC ANEURYSMS»

«ΠΗΚΤΙΚΟ ΠΡΟΦΙΛ ΚΑΙ ΕΚΒΑΣΗ ΣΕ ΕΝΔΑΓΓΕΙΑΚΗ ΑΠΟΚΑΤΑΣΤΑΣΗ ΡΑΓΕΝΤΩΝ ΑΝΕΥΡΥΣΜΑΤΩΝ ΚΟΙΛΙΑΚΗΣ ΑΟΡΤΗΣ»

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ABSTRACT

Background: The aim of this study is to investigate whether preoperative coagulation profile is predictive of outcome in patients undergoing endovascular aortic repair (EVAR) for ruptured abdominal aortic aneurysms (RAAAs).

Methods: Consecutive patients undergoing EVAR for RAAA between March 2010 and December 2016 were recruited from a single vascular unit. Patient details, including fibrinogen levels, platelets count, aPTT and INR levels on admission were extracted from case files. Major outcomes were recorded as: 30-day mortality, mortality overall, major adverse cardiovascular events (MACE), endoleaks and interventions. We used t-test to examine for potential associations.

Results: Thirty patients (29 males, mean 72.9 years), all with available initial coagulation screening were included in this series. Four patients died within 30 days after the procedure (13.3%) and a further 2 died from unrelated causes during the follow-up (median 8 months), raising the overall mortality to 20%. Ten patients suffered a MACE (33.3%), 8 had an endoleak (26.7%) and 5 required an aneurysm-related re-intervention (16.7%). Presenting fibrinogen levels and platelets count were significantly higher in the group of patients surviving 30 days compared to the fatal cases (p=0.044; p=0.022), as well as in those without an endoleak compared to those with an endoleak (p=0.001; p=0.028). Higher presenting platelets count were significantly associated with lower overall mortality rates (p=0.026) whereas patients with higher INR levels had significantly more re-interventions (p=0.044).

Conclusions: In this small series of EVAR for RAAAs, a potential preoperative hypercoagulable profile with higher fibrinogen levels and platelets count may be associated with better chances of early survival and a lower probability of an endoleak at follow-up. Further studies are needed to clarify this issue and possible future therapeutic implications, for example, whether outcome can be improved by technically increasing fibrinogen levels along with the administration of blood products, as soon as the diagnosis of RAAA is made.

ΠΕΡΙΛΗΨΗ

Εισαγωγή: Σκοπός αυτής της μελέτης είναι η πιθανή πρόβλεψη της έκβασης με βάση το προεγχειρητικό πηκτικό προφίλ, σε ενδαγγειακή αποκατάσταση (EVAR) ραγέντος ανευρύσματος κοιλιακής αορτής (ΡΑΚΑ).

Μέθοδοι: Συμπεριλήφθηκαν διαδοχικοί ασθενείς κατά το διάστημα μεταξύ του Μαρτίου του 2010 έως Δεκέμβρη του 2016 από μία αγγειοχειρουργική κλινική. Από τους ιατρικούς του φακέλους καταγράφηκαν λεπτομέρειες σχετικά με τους ασθενείς, συμπεριλαμβανομένων των προεγχειρητικών τιμών ινωδογόνου, αιμοπεταλίων, aPTT και INR κατά την εισαγωγή τους. Τα σημαντικά αποτελέσματα ήταν: η άμεση θνητότητα (30 ημερών), συνολική θνητότητα, κύρια δυσμενή καρδιαγγειακά συμβάντα (ΔΥΚΑΣ), ενδοδιαφυγές και επανεπεμβάσεις. Για τη διερεύνηση των πιθανών σχέσεων χρησιμοποιήθηκε το t-test.

Αποτελέσματα: Τριάντα ασθενείς (29 άντρες, μέση ηλικία=72.9 έτη) συμμετείχαν στη μελέτη. Τέσσερις ασθενείς απεβίωσαν τις πρώτες 30 μετεγχειρητικές ημέρες (13.3%), ενώ 2 ακόμη κατέληξαν από μη σχετιζόμενα αίτια (20%) κατά τη διάρκεια της παρακολούθησης (διάμεσος=8 μήνες). Δέκα ασθενείς υπέστησαν ΔΥΚΑΣ (33.3%), 8 βρέθηκαν με ενδοδιαφυγή (26.7%) και 5 χρειάστηκαν επανεπέμβαση (16.7%). Οι προεγχειρητικές τιμές ινωδογόνου και αιμοπεταλίων ήταν σημαντικά υψηλότερες στους επιζήσαντες σε σχέση με τους θανόντες κατά τις 30 πρώτες ημέρες (p=0.044; p=0.022), καθώς επίσης και στους ασθενείς χωρίς ενδοδιαφυγή (p=0.001; p=0.028). Σημαντικά χαμηλότερα ποσοστά συνολικής θνητότητας παρουσίασαν οι ασθενείς με υψηλότερες τιμές αιμοπεταλίων κατά την εισαγωγή τους (p=0.026), ενώ στατιστικά σημαντική συσχέτιση βρέθηκε μεταξύ των υψηλότερων τιμών INR και των επανεπεμβάσεων (p=0.044).

Συμπέρασμα: Σε αυτή τη μικρή σειρά ασθενών με EVAR για ΡΑΚΑ, πιθανόν ένα προεγχειρητικό υπερπηκτικό προφίλ, με υψηλά επίπεδα ινωδογόνου και αιμοπεταλίων, να συνδέεται με περισσότερες πιθανότητες άμεσης επιβίωσης καθώς και λιγότερες πιθανότητες εμφάνισης ενδοδιαφυγής μετεγχειρητικά. Μεγαλύτερες και περισσότερες μελέτες απαιτούνται για τη διερεύνηση του ζητήματος της συσχέτισης, καθώς και για πιθανές μελλοντικές θεραπευτικές επιλογές όπως η ενδεχόμενη τεχνητή αύξηση των επιπέδων ινωδογόνου ταυτόχρονα με τη χορήγηση προϊόντων αίματος, με τη διάγνωση της ρήξης.

INTRODUCTION

Abdominal aortic aneurysm is a dilatation of the aorta more than 50% of the diameter. Progression and enlargement of the aneurysm can lead to rupture and massive internal bleeding. Ruptured abdominal aortic aneurysm (RAAA) is a lethal condition and remains with high rates of morbidity and mortality of around 50%. [4,6-8,14] Overall population mortality is, however, much higher reaching rates of 80-90%, because less than half of the patients reach hospital alive. [2,15] Open repair (OR) was the standard treatment of RAAAs for more than 50 years, however during the last two decades EVAR has been used around the world with equal results. [13]

EVAR was first described in 1991 by Parodi et al and Volodos et al, and brought a revolution in the minimal invasive approach to elective AAAs. [16-18] Not many years later, in 1994, EVAR was used as potential treatment for RAAAs as well (rEVAR) [19,20], and nowadays has been promoted as treatment of choise. [21]

Several studies have compared emergency OR with rEVAR for RAAA. Several observational studies indicated potential better 30-day survival and complication rates following EVAR for RAAA comparing to OR, but no significant differences in overall mortality. [5,9,11] However, other studies and a randomized controlled trial, did not prove inferiority of EVAR over OR for RAAAs and elective AAAs. [10,12]

Further studied need to be done, to investigate potential preoperative factors that may influence survival and improve outcome in EVAR. Our hypothesis is that coagulation profile factors, comprising fibrinogen levels, platelets (PLT) count, activated partial thromboplastin time (aPTT) and international normalized ratio (INR) levels on admission, might be potential biomarkers predictors of outcome (early or overall) in RAAA patients undergoing EVAR. Increase in levels of these factors may be associated with a hypercoagulable state, which might be protective in RAAAs, and therefore immediate access to coagulation status, as soon as the diagnosis is made, will be very useful. The aim of this retrospective observational study is to investigate potential association between preoperative coagulation profile and outcome in patients treated with EVAR for RAAA.

METHODS AND MATERIALS

Study design

During the study period 1 March 2010 and 31 December 2016 consecutive patients undergoing EVAR for RAAA were enrolled in this retrospective observational study. The study was held in a single vascular unit based on a tertiary university hospital that provided on-call vascular services for northern Greece every fourth day. Our unit started operating electives EVAR back in 1995, and established EVAR protocol for RAAA in early 1998 [1,2], therefore our surgeons have gained a lot of experience in the field, being among the first to operate EVAR for RAAA in Greece. [2,3] Surveillance and follow-up consisted of abdomen X-rays and CT scans before discharge, at 1, 3, 6 and 12 months and annually thereafter for the remaining lifetime of the patient. The study did not require formal ethical approval by the Hospital Ethical Committee and in all cases, relatives and when possible the patients themselves, signed informed

consent form prior to the operation, after discussion of the severity of their condition, poor prognosis and possible complications.

During the study period, a total of 53 patients were diagnosed for RAAA and treated with EVAR. Twenty-three patients were excluded due to lack of records from case files or inadequate presenting coagulation profile screening. Therefore, 30 patients enrolled in this study and no one denied intervention for logistic reasons. Patient details were extracted from case files and information was gathered from medical, nursing, medication and emergency department's records. Demographic data comprised age, sex, date of admission and past medical history records included cardiac disease, hypertension, chronic obstructive pulmonary disease (COPD), cerebrovascular disease (CVD), diabetes mellitus history, smoking status, hostile abdomen and history of previous EVAR (elective or rupture). Other factors contain duration of symptoms, presenting systolic blood pressure, lowest recorded systolic blood pressure, loss of consciousness, hemodynamic instability, type of anesthesia and aneurysm morphological characteristics. Hemoglobin, serum creatinine levels and coagulation profile values on admission, including preoperative fibrinogen levels, platelets count, activated partial thromboplastin time, international normalized ratio levels, were recorded from laboratory database.

Procedure details

As soon as rupture was suspected in the emergency room, the patient was brought straight to the radiology department, for a computed tomography scan (CT). The duration of the whole procedure did not last more than 30 minutes totally. However, when rupture was identified and diagnosed via CT by a referring peripheral hospital, patient was transferred immediately to the operating room bypassing the emergency department (ED). Diagnosis and evaluation of a suspected RAAA was set by contrast-enhanced spiral CT with 5mm slices and was assessed by the on-call radiologist and vascular surgeon. The decision to proceed to EVAR or open repair (OR) was made by the on-call vascular expert, according to their judgement. EVAR is the preferred method of repair in our center, however complexity of anatomy, personal competence and expertise in performing advanced EVAR and hospital resources, were all contributing factors upon deciding the method of repair. Anatomic criteria for EVAR in RAAA patients did not differ from criteria in an elective repair, the most important of them being that the infrarenal neck should have a length of at least 10mm. There were no specific inclusion or exclusion criteria, according to the hemodynamic state of the patient. With gaining experience and expertise throughout the years, more and more challenging cases were treated with endovascular means in our unit, leading to the expansion of selection criteria, both for ruptured EVAR (rEVAR) and elective repair.

When the decision was made about the type of the intervention and the patient was considered suitable for EVAR, they were transferred in a dedicated hybrid vascular operation room, both for endovascular and open procedures. Since a vascular interventional radiologist was not available in our hospital, all endovascular repairs are performed by the on-call vascular team, consisting of one vascular specialist and two vascular trainees. The surgery was usually done under local anesthesia and intravenous sedation was administrated, when needed, to minimize patient movement and discomfort. General anesthesia was chosen in cases where severe hypovolemia caused loss of consciousness or patency of airway was under threat. All

patients were under close monitoring by the anesthesiologist, throughout the intervention. Intravenous fluid and blood resuscitation were kept to a minimum until aneurysm exclusion, to achieve a systolic blood pressure goal of 80-100 mmHg. Access to the common femoral arteries was gained by bilateral skin incisions in the groins and suitably sized sheaths were used to cannulate the femoral arteries. Our endovascular facilities include a mobile C-ARM image intensifier to perform EVAR and other endovascular interventions. In cases of profound intra-operative hemodynamic instability, an aortic occlusion balloon was used selectively to prevent exsanguination. The most important factor for the selection of the stent graft was device availability, as well as surgeon's preference, expertise and aneurysm anatomic and morphological characteristics. Access to stent grafts was through local company representatives.

Inclusion Criteria

Every patient with diagnosed RAAA via CT, defined by International Classification of Diseases (ICD) 10 codes and treated with EVAR during this study analysis, were enrolled in the study. Inclusion criteria comprised only patients with available presenting laboratory values concerning coagulation profile and those who were treated with endovascular means. Therefore, patients without initial ED coagulation screening, those who underwent endovascular repair but switched to open, or those who were treated with open repair (OR) in the first place, were excluded from this analysis.

Outcomes and Definitions

Primary outcome measures were 30-day mortality, summarizing the rate of deaths in the first 30 postoperative days and overall mortality, which included the rate of fatal cases from all-cause mortality, throughout the follow-up period. Secondary outcomes measures comprised endoleaks, major adverse cardiovascular events (MACE) and aortic-related re-intervention. MACE was defined as lower limb amputation, ischemic coronary disease (i.e. MI), cerebrovascular disease (stroke or TIA), aneurysm-related morbidity and/or re-intervention and all-cause mortality as a composite end-point.

Hemodynamic instability was used to describe every patient with hypotension (systolic blood pressure ≤ 80 mmHg) and/or loss of consciousness at any time before the repair. Duration of symptoms was defined as the time passed since the onset of the first clinical sign of rupture (i.e. pain, loss of consciousness, etc.), until the moment patients entered the operating room. Lastly, the term hostile abdomen includes all kind of operations and interventions in the area of the abdomen, including previous EVAR (elective or urgent).

Statistical analysis

All statistical analysis was performed using the IBM® SPSS® Statistics software, Version 23 for macOS (IBM Corp.). Continuous descriptive data are presented as mean ± standard deviation (range) or median (25^{th} percentile [Q1] to 75^{th} percentile [Q3]) for non-normally distributed data, as appropriate. Categorical variables are presented as No. (percentage of total [%]). Continuous data were tested for normal distribution using *Shapiro-Wilk's* test.

Descriptive comparisons of continuous data were performed using *t*-test or the *Mann-Whitney U* test, as required, whereas categorical variables were compared with

chi-square (x^2) test. We performed univariate analysis between major outcomes and data describing coagulation profile. However, we were not able to analyze data using binary logistic regression, because of the limited number of enrolled subjects. Statistical significance level was set to a *p*-value<0.05.

RESULTS

A total of thirty patients (29 males, 1 female) with mean age 72.9 years (range=33, 55-88 years) underwent EVAR for RAAA during this study period. Demographic details, patients' medical history, presenting clinical features and laboratory values, as well as details regarding the surgical procedure are summarized on *Table 1*. Cardiac disease history, including coronary artery disease, cardiac failure and atrial fibrillation, was recorded in 53.3% of patients, while more than 60% of them were under treatment for hypertension and were active or ex-smokers. Chronic obstructive pulmonary disease was observed in 43.3% of study population, 10% had cerebrovascular disease history, including transient ischemic attack (TIA) or stroke, and 30% of them were diabetic. As far as surgical history is concerned, a significant percentage of 50% had hostile abdomen, 8 out of 30 patients (26.7%) had undergo previous EVAR (5 had an elective EVAR and 3 had EVAR for RAAA) and only 1 had been treated with open repair (3.3%).

The median duration of symptoms, until the moment patient arrived at the hospital, was 18 hours (Q1-Q3=21). Four patients (13.3%) arrived with systolic blood pressure (SBP) below 80 mmHg, and the mean presenting SBP was 111.7 (range=150, 30mmHg-180 mmHg). Eight patients (26.7%) lost their consciousness, at least once, prior or after arriving to the emergency department and approximately half of them (46.7%) presented or became hemodynamically unstable during the preoperative management.

Laboratory values included a mean PLT count 225.1 (range=292, 109-401x10^9/L) and mean fibrinogen levels 411.3 (range=808, 133-941 mg/dL). Coagulation mechanism was represented by a median INR 1.15 (Q1-Q3=0.22) and median aPTT 30.1 sec (Q1-Q3=7.87 sec). Mean hemoglobin (Hb) value was 11.1 g/dL (range=7, 8-15 g/dL) and median serum creatinine levels was 1.31 mg/dL (Q1-Q3=0.86 mg/dL).

Seventy percent of the patients during this study period had a de novo RAAA and the mean aneurysm diameter was 8.1 cm (range=8, 4-12 cm). De novo RAAAs were treated with 16 bifurcated stent grafts, 3 aortouniiliac endografts with femoro-femoral crossover bypass and 2 ruptured aneurysms were treated with tube endograft combined with the chimney-periscope technique. Twenty-seven patients (90%) underwent the procedure with local anesthetic in the groins, whereas general anesthesia was used in only three patients (10%).

Table 1: Descriptive data

Variable	**No. (%) or mean/median (range/Q1-Q3)**
Total	30 (100%)
Demographic details	
Sex	
Males	29 (96.7%)
Females	1 (3.3%)
Age (years)	72.9 (33)
Medical history	
History of cardiac disease	16 (53.3%)
Hypertension	19 (63.3%)
Smokers (current or ex)	20 (66.7%)
COPD	13 (43.3%)
CVD (stroke or TIA)	3 (10%)
Diabetes	9 (30%)
Hostile abdomen	15 (50%)
Previous EVAR	8 (26.7%)
Elective	5 (16.6%)
rEVAR	3 (10%)
Previous open repair	1 (3.3%)
Presenting clinical features	
Duration of symptoms (hours)	18 (21)
Presenting SBP (mmHg)	111.7 (150)
Presenting SBP $\leq$ 80 mmHg	4 (13.3%)
Lowest measured SBP (mmHg)	88 (100)
Loss of consciousness	8 (26.7%)
Hemodynamic instability (SBP $\leq$ 80 mmHg± loss of consciousness)	14 (46.7%)
Laboratory values on admission	
PLT count (x10^9/L)	225.1 (292)
aPTT (sec)	30.1 (7.87)
INR	1.15 (0.22)
Fibrinogen (mg/dL)	411.3 (808)

Hb (g/dL)	11.1 (7)
Serum Creatinine (mg/dL)	1.31 (0.86)
Surgery and aneurysm-related details	
Anesthesia	
General	3 (10%)
Local	27 (90%)
Diameter (cm)	8.1 (8)
De novo rupture	21 (70%)

COPD: chronic obstructive pulmonary disease; CVD: cerebrovascular disease; TIA: transient ischemic attack; EVAR: endovascular aneurysm repair; rEVAR: ruptured endovascular aneurysm repair; SBP: systolic blood pressure; PLT: platelets; aPTT: activated partial thromboplastin time; INR: international normalized ratio; Hb: hemoglobin

Major outcomes

Major outcomes are summarized on *Table 2*, along with univariate analysis between the major outcomes and coagulation profile in patients undergoing EVAR for RAAA during this study period. Four patients (13.3%) died during the first 30 postoperative days, two of them intraoperatively due to exsanguination causing cardiac asystole. The other two died in the first 24 hours after the procedure in the intensive care unit (ICU), due to multiple organ failure. The patients received large amounts of blood transfusion, blood products as well as inotropes, however they never recovered from the severe hypovolemic shock, as result of the massive bleeding.

During a median follow up period of 8 months (Q1-Q3=17.7 months), two more patients died from unrelated causes, raising the overall mortality rate to 20%. One patient died from cardiorespiratory failure on 4 months follow up, whereas the other died on 11 months from pancreatic cancer.

Eight patients developed endograft endoleak in the follow-up period (26.7%). In detail, five of them had type Ia, one type Ib, one type II and lastly one came with type III endoleak. Thirty three percent of enrolled patients suffered from MACE (no=10). Details about MACE are thoroughly described on *Table 3*. Lastly, five patients (16.7%) underwent aneurysm-related re-intervention. In detail, one patient underwent re-intervention for type Ib, two patients were treated with aortic cuff for type Ia and one for type III and one more was headed to the theater due to proximal endograft limb retraction that was successfully treated with right iliac endograft limb extension.

Table 2: Univariate association between major outcomes and coagulation profile

Major Outcomes	No. (%)	p-value			
		Fib	**PLT**	**aPTT**	**INR**
30-Day mortality	4 (13.3%)	*0.044*	*0.022*	0.154	0.6
Overall mortality	6 (20%)	0.3	*0.026*	0.352	0.979
Endoleak	8 (26.7%)	*0.001*	*0.028*	>0.99	*0.011*
MACE	10 (33.3%)	0.276	0.862	0.196	0.573
Re-intervention	5 (16.7%)	0.853	0.655	0.25	*0.044*

	mean/median			
	Fib (mg/dL)	**PLT** (x10^9/L)	**aPTT** (sec)	**INR**
30-Day mortality				
survivors vs fatal cases	436 vs 253	237.5 vs 151	30.6 vs 25.7	1.15 vs 1.3
Overall mortality				
survivors vs fatal cases	428 vs 346	240.5 vs 169	30.6 vs 27	1.16 vs 1
Endoleak				
no vs yes	470 vs 249	243.5 vs 179	30.3 vs 30	1.1 vs 1.3
MACE				
no vs yes	436 vs 362.5	227 vs 222	31.5 vs 29	1.15 vs 1.16
Re-intervention				
no vs yes	414 vs 398	222 vs 238	29.8 vs 30.4	1.12 vs 1.2

MACE: Major adverse cardiovascular events; Fib: fibrinogen; PLT: platelets; aPTT: activated partial thromboplastin time; INR: international normalized ratio

Table 3: Major adverse cardiovascular events

MACE	No.
Total	10
Intra-op death	4
MI – 3months post-op	1
Left endograft limb occlusion - right to left femoro-femoral cross over bypass - wound infection and left AKA – 1 week post-op	1
Proximal aortic cuff – 14months follow-up	1
Death from cardiorespiratory failure – 4months follow-up	1
Aortic cuff for type 3 endoleak	1
SFA occlusion causing claudication	1

Intra-op: intraoperative; MI: myocardial infraction; AKA: above knee amputation; post-op: postoperative; SFA: superficial femoral artery

Primary outcomes

According to our univariate analysis, fibrinogen levels were significantly higher in the group of survivors compared to fatal cases during the first 30 postoperative days (mean ± SD: 436±167 mg/dL vs 238±107 mg/dL; p=0.044) (*Figure 1*). Preoperative platelets count also differed significantly between the two groups, being higher in survivors (mean ± SD: 237.5±69 vs 151±29.6; p=0.022) (*Figure 2*). However, aPTT and INR were not found to be significantly associated with early survival.

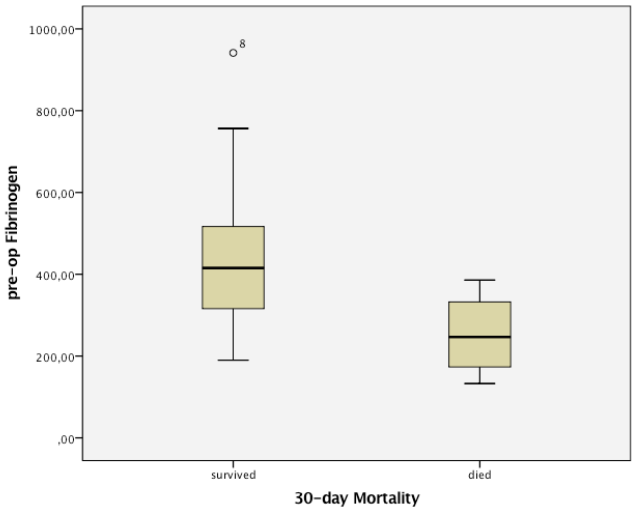

Figure 1: Boxplot of pre-op fibrinogen levels in survivors and fatal cases in the first 30 post-op days.

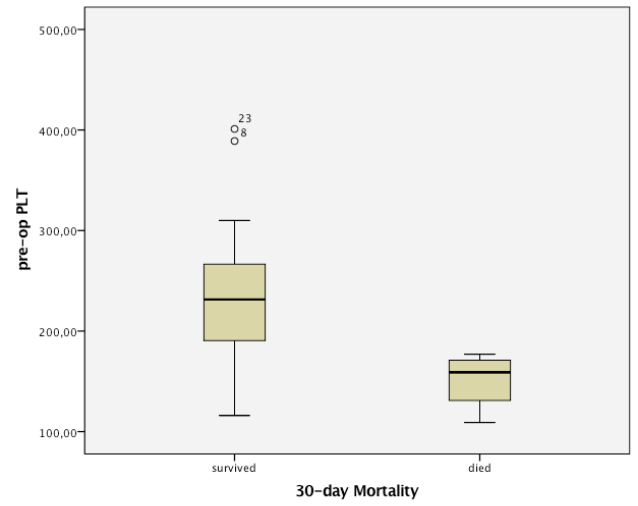

Figure 2: Boxplot of pre-op platelets count in survivors and fatal cases during the first 30 post-op days.

After this early 30-day period of close follow-up, only PLT count seemed to be significantly associated with overall mortality. Platelets count remained significantly higher in those who survived during the median follow-up of 8 months in comparison to the fatal cases (mean ± SD: 240.5±71 vs 169±36; p=0.026) (*Figure 3*). Fibrinogen levels, as well as aPTT and INR were not significantly different between those who survived and died overall.

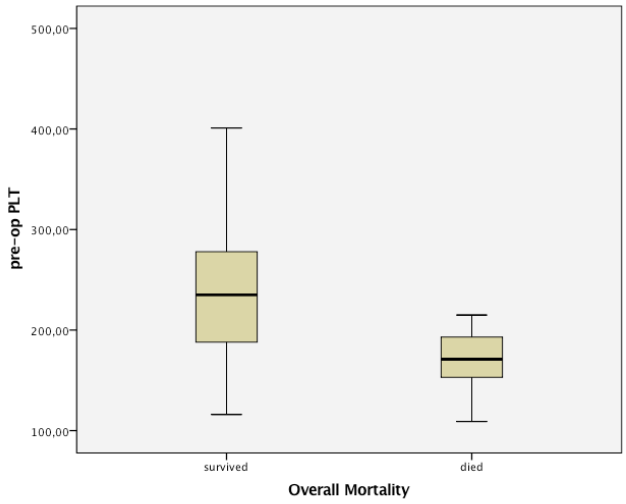

Figure 3: Boxplot of pre-op platelets count of overall survivors and fatal cases.

Secondary outcomes

Preoperative fibrinogen levels, platelets count and INR seemed to be significantly associated with endoleak after EVAR procedure for RAAA in this small series. Fibrinogen levels and platelets count on admission were higher in those without an aortic related endoleak compared to those who developed one (mean ± SD: 470±155 vs 249±87; p=0.001) (mean ± SD: 243.5±68 vs 179±61; p=0.028) (*Figures 4,5*). Contrary, INR was significantly low in patients without and endoleak (median 1.1 vs 1.3; p=0.011) (*Figure 6*), and only aPTT did not differ significantly between the two groups.

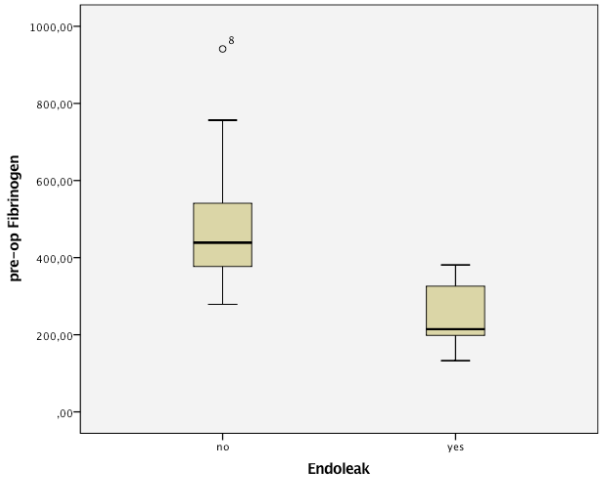

Figure 4: Boxplot of pre-op fibrinogen levels in patients with and without an endoleak.

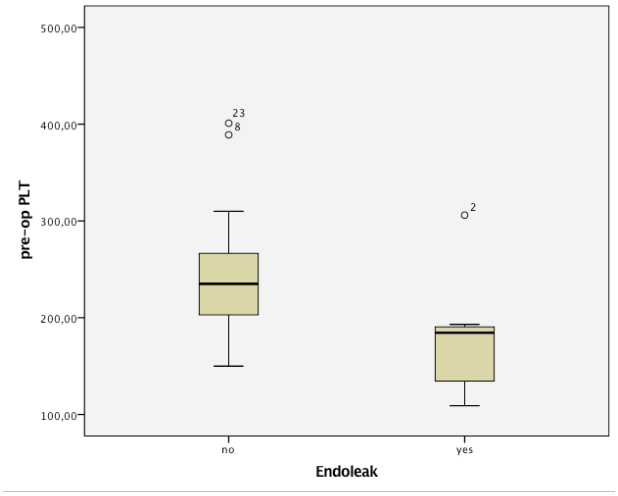

Figure 5: Boxplot of pre-op platelets count in patients with and without an endoleak.

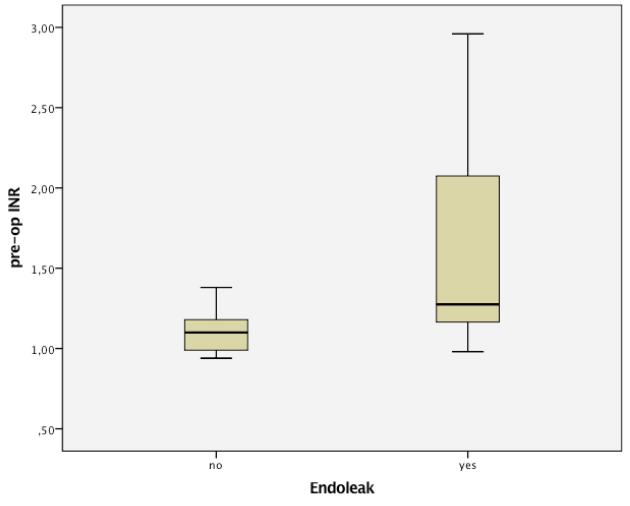

Figure 6: Boxplot of pre-op INR levels in patients with and without an endoleak.

The preoperative variables of patients' coagulation profile we chose to analyze, did not have any statistically significant difference between patients who suffered from MACE and those who did not, during the follow-up.

Preoperative INR levels were slightly significant higher in patients who underwent re-intervention for aneurysm related complications, compared to patients free of re-intervention (median: 1.2 vs 1.12; p=0.044) (*Figure 7*). Presenting fibrinogen, platelets and aPTT values did not seem to be associated with re-intervention.

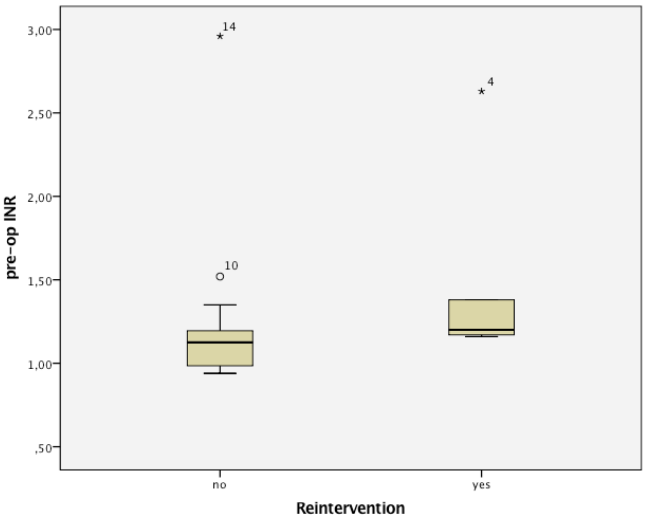

Figure 7: Boxplot of pre-op INR levels in patients with and without an aneurysm related re-intervention.

DISCUSSION

Admiring advances have been made in surgical and anesthetic techniques over the last decades, in the management of acute surgical conditions, such as RAAA. However, perioperative morbidity and mortality rates remain high reaching 50%.[22] EVAR for RAAA is a very difficult and competitive procedure among vascular emergencies, so it of paramount importance the recognition of pre-operative factors that may influence outcome results regarding survival and complications of the intervention.

Major hemorrhage and persisting hypotension after rupture seem to contribute to the raised mortality rates and are believed to be the main cause of intra-operative death. [23] Trauma and hemorrhage are associated with coagulopathy, which nowadays is considered to be the consequence of anticoagulant protein C pathway activation, rather than the consumption as highlighted in earlier studies. [24,25,28,29] Even if patients survive intra-operative danger, post-operative mortality remains high due to the complications following rupture, such as multiple organ failure, myocardial infarction, and thromboembolism. A possible contributing mechanism for these complications is an imbalance between the activation of the coagulation system and the fibrinolytic system.

The coagulation system is activated in patients with RAAA and shock, and the development of coagulopathy predicts poor outcome. Acute traumatic coagulopathy is the failure of coagulation homeostasis, arising rapidly after traumatic injury, hemorrhage, and shock. [28,29] Prolonged prothrombin time, degree of fibrinolysis, depletion of coagulation factors and inhibitors, and general failure of the blood have all been identified as being primary indicators for acute traumatic coagulopathy. [26] There are reports in literature, dating back in early 1990s, that investigated pre-operative coagulopathy in RAAAs. Davies MJ et al concluded in their study, that patients with reduced platelet count (<100 x 10^9/L) or a prothrombin time > 1.5 times the control value, had significantly higher mortality rates when compared to patients with normal screening results (p<0.001). These findings may indicate that

coagulopathy at the time of admission predicts poor outcome in patients with ruptured aortic aneurysm. [23] Another study in the early days of rEVAR, found that continued hemorrhage caused thrombocytopenia at the end of the surgery, which resulted in increased post-operative morbidity and mortality rates. [27] Later, other studies investigated the role of coagulopathy in RAAA and concluded that the majority (85%) of RAAAs do not present with coagulopathy and in those that do so, significant coagulopathy is limited to only 6%. [25] Other reports examined the potential association between emergency department coagulation profile and outcome, and found no significant differences in PT, APTT, platelet count between patients who survived and those who died, therefore coagulation profile is not a predictor of outcome in RAAAs. [30] No statistically significant correlation between preoperative coagulopathy and mortality was found in another study in 2016, although a significantly greater degree of postoperative coagulopathy was seen among patients who died both within 24-h and 30 days postoperatively. [31]. As far as fibrinogen is concerned, low preoperative fibrinogen concentration was significantly associated with preoperative hypotension and increased intraoperative bleeding in patients with RAAA. [32] RAAA repair is associated with inhibition of systemic fibrinolysis and intense thrombin generation. Similar changes are seen in non-ruptured AAA but are of a lesser magnitude. This procoagulant state may contribute to the microvascular and macrovascular thrombosis that leads to myocardial infarction, multiple organ failure, and thromboembolism. [34] A hyperfibrinolytic state was reinforced by shock, however, the clinical outcome with a relatively high incidence of thrombosis-related deaths, indicate a prothrombotic state instead of a hyperfibrinolytic state as a major end-point of attention in patients with shock as a result of a RAAA. [33]

Transfusion in trauma and in shock patients, has been according to practice guidelines. [35,36] Proactive administration of PLT and Fresh Frozen Plasma (FFP) improves coagulation competence, reduces postoperative hemorrhage, increases survival in massively bleeding RAAA patients and smaller FFP/RBC ratios (RBC: red blood cells) and larger volumes of crystalloid infusion were associated with development of coagulopathy and poorer prognosis of survival. [31,37] In another study, EVAR patients treated with massive transfusion (MT) had lower FFP/RBC and PLT/RBC ratios than OR patients with MT for RAAA. [38]

In this small series analysis, we attempted to investigate the association between presenting coagulation screening and outcome in patients undergoing EVAR for RAAA. Fibrinogen levels and PLT count on admission seemed to be significantly associated with better chances of 30-day survival and fewer endoleaks rates. The latter was, also influenced by lower INR levels. Only, higher presenting PLT count may be predictive of overall survival in these patients. Coagulation profile failed to predict MACE during follow-up period. Lastly, patients who underwent aneurysm-related re-intervention, presented with prolonged INR values.

The present study has certain limitations. It is a retrospective study that suffers from small numbers. This kept us from using important analysis methods, such as logistic regression. Nevertheless, this is an important pilot study and the results should be taken into account for future and larger studies.

Conclusion

In conclusion, higher fibrinogen levels and PLT count on admission, which may indicate a preoperative hypercoagulable and prothrombotic profile may be associated with better chances of early survival in RAAA patients undergoing EVAR. Whether the outcome of these patients can be improved by technically increasing fibrinogen levels through proactive administration of plasma, FFP or other blood products, as soon the diagnosis of RAAA is made, remains to be seen.

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